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09/957,031	09/21/2001	David Margolis	BSZ-008DV	6530

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LAHIVE & COCKFIELD, LLP.  
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EXAMINER

SULLIVAN, DANIEL M

ART UNIT PAPER NUMBER

1636

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/957,031

Applicant(s)

MARGOLIS ET AL.

Examiner

Daniel M Sullivan

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 89-139, 141-147, 161-168 and 179-190 is/are pending in the application.
- 4a) Of the above claim(s) 101-108, 129-136 and 161-168 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 89-100, 109-128, 137-139, 141-147 and 179-190 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

This Office Action is a reply to the Paper filed 21 April 2004 in response to the Non-Final Office Action mailed 16 October 2003. Claims 101-108, 129-136 and 161-168 had been withdrawn from consideration and claims 89-100, 109-128, 137-160 and 169-190 were under consideration in the 16 October Office Action. Claims 140, 148-160 and 169-178 were canceled and claims 188-190 were amended in the 21 April Paper. Claims 89-139, 141-147, 161-168 and 179-190 are pending and claims 89-100, 109-128, 137-139, 141-147 and 169-190 are under consideration.

### ***Response to Amendment***

Rejection of claims 140, 148-160 and 169-178 is rendered moot by the cancellation thereof.

### **Claim Rejections - 35 USC § 112**

Rejection of claims 188-190 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment thereof such that the methods are limited to *in vitro*.

### **Claim Rejections - 35 USC § 103**

Claims 89-100, 109, 111-115, 117-128, 137, 141-145 and 179-190 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wiener *et al.* (U.S. Patent 6,342,390, filed November 23, 1994) in view of Mannino and Gould-Fogerite (1996; WO 96/25942) for reasons of record and herein below in the response to arguments.

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***Response to Arguments***

Claims 89-100, 109, 111-115, 117-128, 137, 141-145 and 179-190 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiener *et al.* in view of Mannino and Gould-Fogerite.

In response to the *prima facie* case and arguments of record, Applicant acknowledges that Mannino teaches that cochleates can successfully deliver nucleic acids and polypeptides. However, Applicant argues that Mannino does not teach or suggest a vector delivery system (including an integrative DNA vector recognized and bound to proteins to facilitate integration) in a manner that will allow for integration of the DNA into the host DNA.

This argument is not persuasive because Mannino is not relied upon to teach a vector delivery system, which is found in the teachings of Weiner *et al.* Applicant is reminded, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Next, Applicant reasserts the contention that the skilled artisan “did not necessarily have a reasonable expectation of success that a vector delivery system could be incorporated within the minimal space available between lipid bilayers of a cochleate.” Applicant urges that, “a skilled artisan did not necessarily have a reasonable expectation of success that the vector delivery system could be properly incorporated into the cochleate in a form conducive to ultimately allow for integration of the DNA within the host DNA” and speculates that the skilled artisan might expect that integrating proteins would be forced to assume a conformation within the minimal space available in the cochleate that would render the invention inoperable or may

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not necessarily have expected that the vector delivery system could be delivered in an active form when carried in the substantially water free cochleate.

These arguments are also not persuasive. There is no evidence of record that would lead one of ordinary skill to the conclusions asserted by Applicant. Applicant acknowledges that Mannino *et al.* teaches that cochleates can successfully deliver both nucleic acids and polypeptides individually. Thus, in order to question the operability of cochleates as a delivery vehicle for the vector delivery structure of Wiener *et al.*, one must have reason to believe either that cochleates generally disrupt protein structure and function, which would seem inconsistent with Applicant's own assertions of general enablement in Mannino *et al.*, or that the vector delivery structure of Wiener *et al.* is particularly affected by the cochleate structure. However, nothing of record would lead one of ordinary skill to believe that either scenario is true.

Applicant particularly identifies the "minimal space available between lipid bilayers of a cochleate" as supporting a lack of reasonable expectation of success, but fails to provide any meaningful definition of "minimal space". Is applicant asserting that the skilled artisan would understand that the space available between lipid bilayers of a cochleate is quantitatively smaller than the delivery structure of Wiener *et al.*, or just that the space is significantly less than the interior of a liposome? However, there is nothing of record to indicate that the former is the case, and if the latter is the case Applicant's argument is analogous to arguing that one would not expect an object that fits within the Taj Mahal to fit inside a mailbox because the Taj Mahal is much bigger. Obviously it is the size of the object relative to its container, not the size of one container relative to another container that is probative.

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Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole; therefore, the claims stand rejected under 35 U.S.C. §103 as obvious over the art.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 110, 116, 138, 139, 146 and 147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiener *et al.* (*supra*) in view of Mannino and Gould-Fogerite (*supra*).

Although the rejection set forth in the previous Office Action was not applied to the claims, upon further review, it is clear that they are obvious over the cited art. Claims 110, 116, 138 and 146 are drawn to the compositions or methods of claims 89, 111, 117 and 141, respectively, wherein the target cell is a pluripotent stem cell. As described in previous Office Actions and herein above, Wiener *et al.* and Mannino *et al.* teach all of the limitations of claims 89, 111, 117 and 141, provide motivation to combine the teachings to produce the instant claimed invention and a reasonable expectation of success. With regard to the composition claims which limit the host cell into which integration of the nucleotide sequences is facilitated to a pluripotent stem cell, the instant specification provides no teaching as to how a composition having that property would differ from a composition wherein the host cell into which integration of the nucleotide sequences is facilitated is not a pluripotent stem cell. In other words, based on the teachings set forth in the specification, it would seem that a composition that facilitates integration of a nucleotide sequence into the genome of a pluripotent stem cell is the

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same as a composition that facilitates integration of a nucleotide sequence into the genome of any other cell. Therefore, the composition of claims 110 and 116 are the same is the same as the composition of the rejected base claims and, therefore, the claims are obvious over the art for the reasons of record.

Furthermore, in the discussion in the first full paragraph in column 5, which is directed to the inclusion of molecules capable of targeting constructs to specific cell types, Wiener *et al.* contemplates the use of CD34 ligand to target hematopoietic progenitor cells, which are known in the art to be pluripotent. As Wiener *et al.* explicitly contemplates targeting pluripotent hematopoietic progenitor cells, the method of claims 138 and 146 would also be obvious to one of ordinary skill in the art at the time the application was filed for the reasons set forth in the *prima facie* case of the Office Action mailed 5 November 2002 regarding claims 117 and 141, and the arguments of record.

Claims 139 and 147 depend from rejected claims 117 or 138 and 141 or 146, respectively, and limit the methods therein to being performed in the absence of cytokine stimulation. Although neither Wiener *et al.* nor Mannino and Gould-Fogerite explicitly teach this limitation, neither do they teach that the methods disclosed therein should be performed in the presence of cytokine stimulation. Thus, absent evidence to the contrary, one of ordinary skill in the art would understand that the methods of Wiener *et al.* and Mannino and Gould-Fogerite are performed in the absence of cytokine stimulation, and, therefore, the methods of claims 139 and 147 would be obvious to one of ordinary skill in the art at the time the application was filed for the reasons of record regarding claims 117 or 138 and 141 or 146.

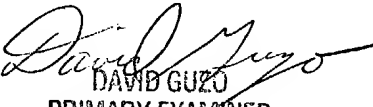
***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M Sullivan, Ph.D.  
Examiner  
Art Unit 1636

  
DAVID GUZO  
PRIMARY EXAMINER